US Army Medical Research and Materiel

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DNA Vaccines Against Hantavirus Infections

This invention provides a recombinant DNA vaccine that uses naked DNA to express individual hantavirus genome segment cDNAs. The approach mimics the *de novo* antigen production and major histocompatibility complex (MHC) class I-restricted antigen presentation that is obtained with live vaccines, without the risk of pathogenic infection.

There are four hantaviruses associated with hemorrhagic fever with renal syndrome (HFRS), including Seoul virus (SEOV), Puumala, Hantaan, and Dobrava-Belgrade viruses. The hantaviruses are usually carried by a single rodent host species. SEOV is the most disseminated hantavirus because its host, the common urban rat, occurs worldwide. The hantaviruses are enveloped and contain a genome comprised of three single-stranded RNA segments designated large (L), medium (M), and small (S) based on size. HFRS vaccines developed and tested in Asia are rodent brain-derived or cell culture-derived, inactivated virus preparations. The inactivated vaccines require growth of the infectious hantavirus in containment laboratories, and present a risk of incomplete inactivation. A vaccinia-vectored vaccine developed in the U.S. was also tested in humans. The recombinant vaccinia virus vaccine has disadvantages including the potential for disseminated infection, especially in immunocompromised individuals, since the vaccine consists of a live virus. Disadvantages common to live virus vaccines also include the potential for lesions containing the infectious virus, [illegible]ort due to swollen lymph nodes, and scarring at the inoculation site.

The invention could be adapted for delivery to epidermal or mucosal tissue, or peripheral blood cells, and thus [illegible]duce humoral, cell-mediated, and secretory responses in the vaccinated individual.

Features and advantages:

- **Elicits SEOV-specific neutralizing antibody responses in rodents**
- **Prevents infection of vaccinated rodents by SEOV, Hantaan, and Dobrava viruses**
- **Growth or use of hantavirus is not required, thus avoiding accidental aerosol transmission**
- **Could potentially deliver via needle, oral, pulmonary, or particle bombardment**

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